TECH CENTER 1600/2900

PTO/SB/08A. (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if Kn wn Substitute for form 1449A/PTO **Application Number** 10/087,951 INFORMATION DISCLOSURE 03/05/2002 Filing Date Donald L. Barbeau STATEMENT BY APPLICANT First Named Inventor 1751 **Art Unit** (use as many sheets as necessary) Examiner Name Barbeau 0302 Attorney Docket Number Sheet of

	 	U.S. PAT	ENT DOCUMEN	TS			
Examiner Initials	 <u>Document Number</u> Number - Kind Code <sup>2</sup> (If known	Publication Date MM-DD-YYYY	Name of Par Applicant of Cite		ent (	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
RR	US- 2,484,029	10/11/1949	Hartman et al.	1260	1250	page 2,col 4; page 3, col 5	
KK _	 us- 3,840,539	10/08/1974	Ueno et al.	260	1250	page 1, col 1-2	
<b>B</b> 35	US- 4,061,636	12/06/1977	Wise et al.	260	1250		
RK	US- 4,757,142	06/12/1988	Pinza et al.	544	129		
RR	US- 4,002,753	01/11/1977	Carpi et al.	424	1250		
KJS	US- 3,978,057	08/31/1976	Anderson et al.	260	1250		
R <sub>2</sub>	US. 4,478,837	10/23/1984	Schenker	424	250		
	 US-				·		
	us-			<u> </u>		RECEIV	F
	US-						L
	US-					AIOV-0	
	 US-					NOV 2 6 20	J2
	 US-					·	
	US-					TC 174	U
	US-					101.	
	 US-						
	 US-						
	 US-	·					
	 US-						
	US-						

	FOREIGN PATENT DOCUMENTS									
Examiner Initials	Cite No.1	Foreign Patent Document  Country Code 3 - Number 4 - Kind Code 9 (f known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	₹6				
	_					-				
						_				

		1	
Examiner Signature	Rounal	Date Considered	1-7-04

English language Translation is addiction.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>&</sup>lt;sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.





PTO/SB/08B (10-01)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE and the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB ontrol number.

Substitute for form 1449B/PTO

TRATE TRAD

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)
Sheet 2 of 4

Complete if Known						
Application Number	10/087,951					
Filing Date	03/05/2002					
First Named Inventor	Donald L. Barbeau					
Group Art Unit	1751					
Examiner Name						
Attorney Docket Number	Barbeau 0302					

Examiner nitiels	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	
кR		DRUERY, J. AND MARXER, A. Hypotensive Hydrazinopthalines and Related Compounds, Journal of Medicinal and Pharmaceutical Chemistry 1(1): 1-21 (1959) Johnson Reprint Corporation New York	
KIZ		SHEPHERD, A. et al. Hydralzine kinetics after single and repeated oral doses, Clinical Pharmacology and Therapeutics 28(6): 804-811(1980)	
1515		LUDDEN, T.M. et al. Hydralazine kinetics in hypertensive patients after single intravenous administration, Clinical Pharmacology and Therapeutics 28(6): 736-742(1980)	
135	-	HAEGELE K.D. et al. Quantitative Analysis of Hydralzine Pyruvic Acid Hydrazone, The Major Mwetabolite of Hydralazine Journal of Chromatography 187:171-179 (1980)	
RR		CLEMENTI, W.A. et al. Endogenous Generation of Hydralazine form Labile Hydralazine Hydrazones, Journal of Pharmacology and Experimental Therapeutics 222(1):159-165 (1982)	
195		OGISO, T. et al. Pharmacokinetics of Formation and Excretion of Some Metabolites of Hydralazine and Their Hypotensive Effect in Rats, Journal of Pharmacology and Experimental Therapeutics 233(2):485-490 (1985)	
1915		IWAKI, M. et al. In Vitro Kinetic Studies of the Reaction of Hydralazine and its Acetone Hydrazone with Pyruvic Acid, Journal of Pharmaceutical Sciences 77(3):280- 283 (1988)	
1315		McLEAN, A.J. et al. Interaction of Hydralazine and Hydrazone Derivatives with Contractile Mechanisms in Rabbit Acartic Smooth Muscle, Journal of Pharmacology and Experimental Therapeutics 205(2): 418-425 (1978)	
1515		HAEGELE, K.D. et al. Identification of Hydrallazine and Hydrallazine Hydrazone Metabolites in Human Body Fluids and In Vitro Comparisons of their Smooth Muscle Activity British, Journal of Clinical Pharmacology 5:489-494 (1978)	
14,		BARRON, K. et al. Comparative Evaluation of the in vitro Effects of Hydralazine and Hydralazine Acetonide on Arterial Smooth Muscle, British Journal of Pharmacology 621:345-349 (1977)	
1815	_	ISRAILI, Z.H. and DAYTON, P.G. Metabolism of Hydralazine Drug, Metabolism Reviews 6(2):283-305 (1977)	-

Examiner	15/5	Date	1-7-11
Signature	1 (Cumul	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

**TE**CH CENTER 1600/2900



Approved for use through 10/31/2002, OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if Known Substitute for form 1449B/PTO 10/087,951 Application Number INFORMATION DISCLOSURE 03/05/2002 Filing Date Donald L. Barbeau First Named Inventor STATEMENT BY APPLICANT Group Art Unit 1751 **Examiner Name** (use as many sheets as necessary) Attorney Docket Number | Barbeau 0302 of

Examiner nitials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), oublisher, city and/or country where oublished.
ÞΩ		O'DONNELL, J.P. et al. Kinetic Studies of Hydralazine Reaction with Acetaldehyde, Journal of Pharmaceutical Sciences 68(10): 1256-1258(1979)
P		ZIMMER, H., A Major Metabolit of 1-Hydrazinophthalazine, Arzeim-Forsch 20(10):1586-1587 (1970)
191)	-	TALSETH, T. Pharmacokinetics and Cardiovascular Effects in Rabbits of a Major Hydralazine Metabolite, the Hydralzine Pyruvic-Acid Hydrazone 211(3):509- 513 (1979)
RP		McLEAN,A.J. et al. Study of In Vitro Effects of Hydralazine Metabolites -Comparative Evaluation of Products of Hydroxylation, Hydrolysis and Conjguation, Archives Instructional Pharmacodynamics 235:19-25 (1978)
RP		LaCAGNIN, L.B. et al. Metabolic Activation of Hydralazine by Rat Liver Microsomes, Blochemical Pharmacology 36(16): 2667-2672 (1987)
1818		LESSEN, T. A et al. Interactions between Drug Substances and Excipients. 1. Fluorescence and HPLC Studies of Triazophthalazine Derivativces from Hydralazine Hydrochloride and Starch Journal of Pharmaceutical Sciences 85(3): 326-329 (1996)
RIZ		SCHNECK,D.W. et al. Plasma levels of free and acid-labile hydralazine: Effects of multiple dosing and of procalnamide Clinical Pharmacology and Therapeutics 24(6): 714-719 (1978)
K15		TALSETH T. et al. Hypotensive Effect of the Hydralazine-Acetone Hydrazone in Conscious Rabbits: Evidence for its Back-Conversion to Hydralazine In Vivo , Journal of Cardiovescular Pharmacology 4: 370-374 (1982)
ΚĶ		McLEAN, A.J. et al. Comparative Evaluation of the Hypotensive Activity of Two Major Metabolites of Hydralazine (1-Hydrazinophthalazine) European Journal of Drug Metabolism and Pharmacokinetics 1: 17-20 (1977)
7)(/		JUCHAU, M.R. AND HORITA, A. Metabolism of Hydralazine Derivatives of Pharmacological Interest, Drug Metabolism Reviews 1(1): 71-100 (1972)
195		HAEGELE, K.D. et al. Determination of Hydralazine and its Metabolites by Gas Chromatography-Mass Spectrometry Journal of Chromatography 126:517-534 (1976)

Examiner	15160000	Date	1-7-0-1
Signature	1/1(anny	Considered	, , ,

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English tanguage Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the Individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



NOV 2 5 2002	<u>.                                    </u>	Paperwork Reduction	on Act of	1995, no persons are requ	U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCI equired to respond to a collection of information unless it contains a valid OMI			
A THAT	Substitute	or form 1449B/PT	0		Complete if Known			
	1	• • • • • • • • • • • • • • • • • • • •	-		Application Number	10/087,951		
	INFOR	RMATION	i dis	CLOSURE		03/05/2002		
	STAT	EMENT D	<b>2V</b> A	PPLICANT		Donald L. Barbeau		
	SIMI	EMEN E	) I M	PPLICANT	Group Art Unit	1751		
	1	(use as many s	heets a	s necessary)	Examiner Name			
	Sheet	4	of	4	Attorney Docket Number	Barbeau 0302		

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where nublished.	T <sup>2</sup>
1517		LUDDEN et al, High-Pressure Liquid Chromatography Assay for Hydralazine In Human Plasma, Journal of Pharmaceutical Sciences 63(11) 1423-1425(1979)	
136		O'DONNELL, J.P., et al., High-Pressure Liquid Chromatography Studies of Reaction of Hydralazine in with Biogenic Aldehydes and Ketones, Journal of Pharmaceutical Sciences 68(12) 1524-1526(1979)	
M		REECE, P.A., et al. Selective High-Performance Liquid Chromatographic Assays for Hydralazine and it Metabolites in Plasma of Man, Journal of Chromatography 181:427-440 (1980)	
132		LACAGNIN, L.B. Separation and Quantitation of Hydralazine Metabolites by High-Performance Liquid Chromatogaphy, Journal of Chromatography 377:319-327 (1986)	
145		IWAKA, M. ET AL. Pharmacokinetics and Biotranformation of Hydralazine Acetone Hydrazone, a Metabolite of Hydralazine, in the Rat , Journal of Pharmaceutical Sciences 78(10):867-873(1989)	
PY'		KANAZAWA, H. et al. New Degradation Products in an Aqueous Solution of Hydralazine Hydrochloride with Cimetidine, Chem. Pharm. Bull. 34(4(:1840-1842 (1986)	
财		SCHULER, W. AND WYSS. E., Zur Frage Der Spezifitat Der Wirkung Blutdrucksenkender Und Rerpinpin-AntagonistichArch. Int. Pharmacodyn. CXXVIII(3-4):431- 468 (1960)	C
*			171
			d
		`	
		·	

Examiner	1 1 1 count	Date	1-7-01
Signature	1 1 20010	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Oraw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the Individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, OC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.